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We theoretically study kinetics of a polymer threading through a pore embedded in a flat membrane. We numerically solve three coupled kinetic equations for the number n_1 of polymer segments in one side of the membrane and expansion factors of the polymer chain in each side of the membrane. We find the time evolution $n_1 \propto t^{1/(1+\nu)}$ at late stages and the translocation time τ_t is scaled as $\tau_t \propto n^{1+\nu}$ for large number n of the polymer segments, where ν is the effective size exponent of the radius of gyration of the polymer. When the polymer is translocated into a region with a good solvent condition ($\nu = 3/5$), we obtain $n_1 \propto t^{5/8}$ and $\tau_t \propto n^{8/5}$. © *2004 American Institute of Physics.* [DOI: 10.1063/1.1800933]

I. INTRODUCTION

Threading of a polymer through narrow channels and pores in a membrane plays an important role for many biological processes[1] and for biotechnologies such as drug delivery and gene therapy. Examples include the translocation of RNA through nuclear pores[2] and the incorporation of membrane proteins into lipid bilayers.[3] Recent experiments have shown that it is possible to drive single stranded DNA and RNA through a narrow channels (or pores) by applying an electric field.[4,5] Although the actual system is complicated by many biological factors, a simple model in which a linear polymer chain translocates through a pore embedded in an impenetrable wall provides useful insights into understanding basic physics of a polymer threading membrane.

Theoretical studies[6–15] have described the polymer translocations as one-dimentional diffusion processes[6] and the nucleation model[8] through a pore embedded in a flat membrane. Sung and Park[6] have studied the transport of a Gaussian chain under the special conditions where the segment friction across the pore is proportional to the polymer length. Muthukumar[8] has treated the process with classical nucleation theory in which the monomer friction is taken to be dictated by the ratchet potential associated with the pore. Recent simulation studies[10,12] with the three-dimentional model have showed that it is possible to capture many essential features of the translocation process using an appropriate one-dimentional model. DiMarzio and Mandell[16,17] have considered the equilibrium properties of a polymer molecule whose two ends reside on opposite sides of a membrane or partition separating two solutions in the limit of no self-excluded volume. In our previous study,[18] we have considered the equilibrium properties of a polymer threading through a narrow pore, coupled to coil-globule transitions of a single polymer chain and predicted a first-order phase transition of a polymer threading a membrane.

In this paper we consider the kinetics of a polymer threading a membrane, based on our previous model.[18] We consider here the late stage where polymer segments are distributed on both sides of the membrane. We propose simple Langevin type's equations for the translocation process, where the friction constant depends on the radius of gyration of the polymer chain as in the Zimm model, and numerically solve three coupled kinetic equations for the number n_1 of polymer segments in one side of the membrane and expansion factors of the polymer chain in each side of the membrane. We study the time evolution of the polymer segments threading a pore and find some scaling behaviors.

II. PHASE TRANSITIONS OF A POLYMER THREADING A MEMBRANE

In this section we introduce the mean field theory to describe the equilibrium properties of a polymer threading a pore.[18] The segments of the polymer on one side (side 1) of the membrane can translocate into the other side (side 2) only by going through this pore whose diameter is comparable to the size of the chemical repeat units on the polymer. We here assume that the chain is tethered to the membrane. In a thermal equilibrium state, the monomer segments are divided among side 1 and side 2. Figure 1 shows a state of a polymer threading membrane, which includes nonequilibrium and equilibrium states. To derive the equilibrium conformation of the polymer and the fraction of polymer segments on each side of the membrane, we consider the thermodynamics of the system based on the Flory-Huggins theory for polymer solutions.[19]

Let n be the number of segments (each of size a) on a polymer and n_1 and n_2 are the numbers of segments on side 1 and 2, respectively. The polymer chain can translocate through a membrane with finite thickness corresponding to an_0. Then we have $n = n_0 + n_1 + n_2$. The free energy of the polymer chain is given by

$$F = F_1 + F_2 + F_0, \tag{1}$$

where F_1 (F_2) shows the free energy of the polymer on side 1 (side 2) and F_0 is the free energy of the segments in the pore.

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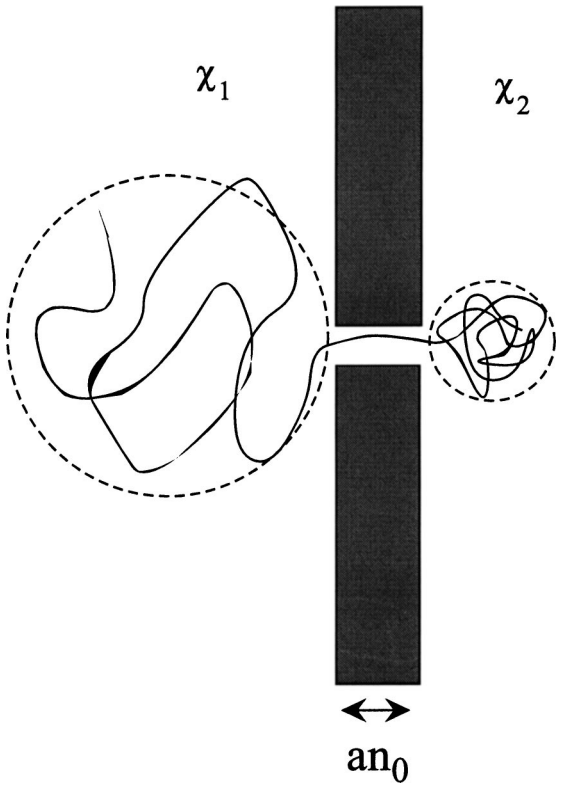

FIG. 1. A polymer molecule consisting of n monomers is threaded through a pore in a flat membrane. The hole is sufficiently small that double threading does not occur.

Let R_1 (R_2) be the mean radius of the occupied region of the monomer segments on side 1 (2). Then the volume fraction of the segments in the sphere R_i is given by

$$\phi_i = \frac{4}{3}\pi a^3 n_i \Big/ \left(\frac{4}{3}\pi R_i^3\right) = a^3 n_i / R_i^3, \tag{2}$$

where $(4/3)\pi a^3$ corresponds to the volume of an unit segment on the polymer. Hereafter the suffix i shows side 1 or 2 ($i=1,2$). We here define the expansion factor α_i of the polymer chain in region i as

$$\alpha_i = R_i / R_{0,i}, \tag{3}$$

where $R_{0,i} = a\sqrt{n_i}$ is the radius of gyration of the ideal chain with n_i segments. The volume fraction, Eq. (2), of the monomer segments in the sphere R_i is then given by

$$\phi_i = \frac{1}{\alpha_i^3 \sqrt{n_i}}. \tag{4}$$

The presence of the surface (membrane) may change the polymer conformation. The chain is stretched by a factor $\sqrt{2}$ in the perpendicular direction.[20] In our model, we neglect the stretching of the chain near the wall.

The free energy F_i on side $i(=1,2)$ is given by

$$F_i = F_{i,el} + F_{i,mix}, \tag{5}$$

where $F_{i,el}$ shows the elastic free energy due to the deformation of the segment distribution from the ideal state. This free energy is given by Flory:[19]

$$\beta F_{i,el} = 3[\tfrac{1}{2}(\alpha_i^2 - 1) - \ln \alpha_i], \tag{6}$$

where $\beta \equiv 1/k_B T$, T is the absolute temperature, k_B is the Boltzmann constant. The second term in Eq. (5) shows the free energy for a mixing of a polymer chain with solvent molecules on side i and is given by the Flory-Huggins theory,[19]

$$\beta F_{i,mix} = \frac{R_i^3}{a^3}[(1-\phi_i)\ln(1-\phi_i) + \chi_i \phi_i (1-\phi_i)], \tag{7}$$

where χ_i shows the Flory-Huggins interaction parameter between a polymer segment and a solvent molecule on side (i). The translational entropy term $(\phi_i/n)\ln\phi_i$ of the polymer chain can be neglected since the center of gravity of the polymer chain is fixed near a membrane in a thermal equilibrium state. The prefactor R_i^3/a^3 is the total number of unit cells in the sphere of the radius R_i.

The free energy F_0 of the segments in the pore is simply given by

$$\beta F_0 = \beta \epsilon_0 n_0, \tag{8}$$

where ϵ_0 is the interaction energy between a polymer segment and a pore. We here assume that the diameter of the pore is of the order of the segment on the polymer. Then we can choose the value of n_0 as one numerical parameter characterizing the thickness of the membrane. In this assumption, the free energy Eq. (8) becomes a constant.

When the interaction energy between a polymer segment and a pore is weak, the polymer can escape completely from the vicinity of the membrane (or either side) because of the conformational entropy of the chain. In our model, however, the chain is tethered to the membrane. This would occur for a polymer chain which has a large end group on the both ends.

In a thermal equilibrium state, the expansion factors α_i of the polymer in side $i(=1,2)$ are determined by minimizing the free energy (1) with respect to α_i:

$$(\partial F/\partial \alpha_1)_{\alpha_2, n_1} = 0, \tag{9}$$

$$(\partial F/\partial \alpha_2)_{\alpha_1, n_1} = 0. \tag{10}$$

The number n_1 of the segments in side 1 is determined by

$$(\partial F/\partial n_1)_{\alpha_2 1, \alpha_2,} = 0, \tag{11}$$

where we have used $n_2 = n - n_0 - n_1$ before the differentiation. The volume fractions are given by

$$\phi_1 = \frac{1}{\alpha_1^3 \sqrt{n_1}}, \tag{12}$$

$$\phi_2 = \frac{1}{\alpha_2^3 \sqrt{n - n_0 - n_1}}. \tag{13}$$

The equilibrium values of α_1, α_2, and n_1 are determined from the three coupled Eqs. (9), (10), and (11).

Here we show some results of our theory.[18] We here put $n_0 = 1$ and assume that the value of the parameter χ_2 in region 2 remains a constant when the parameter χ_1 in region

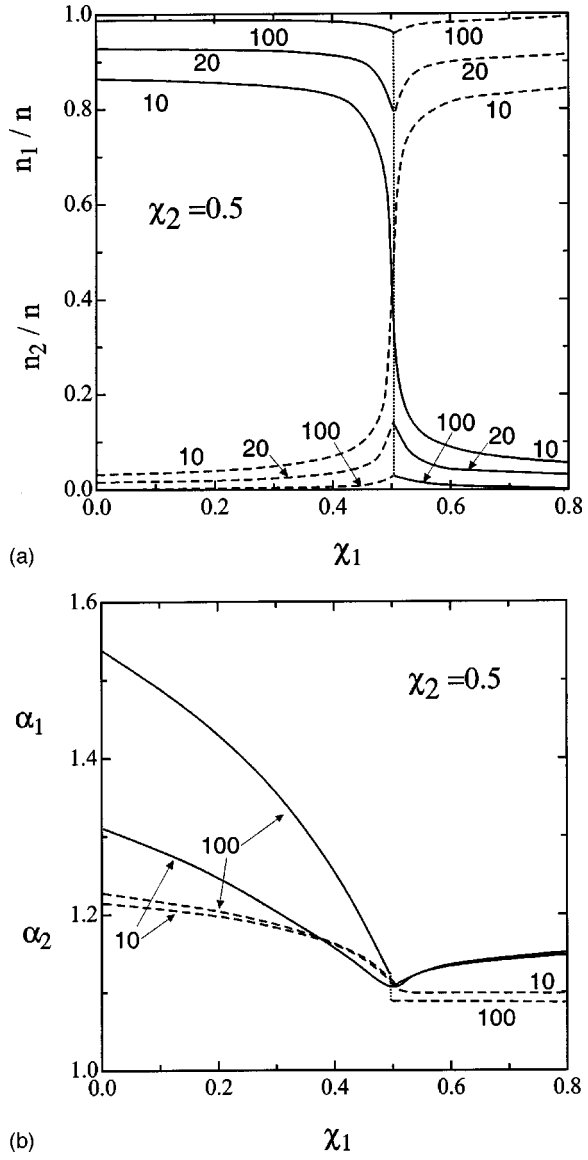

FIG. 2. (a) The solid curve shows the fraction n_1/n and the dashed curve corresponds to n_2/n plotted against χ_1 with $\chi_2=0.5$ for various values of n. (b) The expansion factor plotted against χ_1 with $\chi_2=0.5$ for $n=10$, 100. The solid curve shows the expansion factor α_1 and the dashed curve corresponds to α_2.

1 is changed. The Flory-Huggins parameter χ can be changed by pH, ionic strength, solvent conditions, and temperature.[19]

Figure 2(a) shows the fraction of polymer segments on each side of the membrane plotted against χ_1 with $\chi_2=0.5$. The number n of the segments on the polymer is changed. The solid curve shows the fraction n_1/n and the dashed curve corresponds to n_2/n. For $n=10$, the fraction of polymer segments in region 1 is continuously decreased with increasing χ_1 and the polymer segments in region 1 are translocated into region 2 through a hole in the membrane. For larger values of n, we find the first-order phase transition of the polymer threading a membrane. When the solvent condition becomes poorer, the polymer segments of a short polymer chain are continuously translocated into region 2. Figure 2(b) shows the expansion factors of the polymer chain on each side of the membrane plotted against χ_1 with $\chi_2=0.5$ for $n=10,100$. The solid curve shows the expansion factor α_1 and the dashed curve corresponds to α_2. On increasing χ_1, the value of the expansion factor α_1 is decreased and slightly jumps at $\chi_1=\chi_2=0.5$. As shown in Fig. 2(a), the value of the fraction n_1 is almost constant when $\chi_1<0.5$ and drastically changed near $\chi_1=\chi_2=0.5$. The polymer chain in region 1 is condensed with increasing χ_1 and most polymer segments remain in region 1 for $\chi_1<\chi_2$. At $\chi_1=\chi_2=0.5$, the polymer segments in region 1 are translocated into region 2.

III. KINETICS OF A POLYMER THREADING A PORE

In this section we study the kinetics of a polymer threading a pore imbedded in a membrane by using our free energy function (1). We here assume that the thickness of the membrane is small ($n_0=1$) and consider a case where the polymer segments are distributed on both sides of the membrane. In a nonequilibrium state, i.e., when $\partial F/\partial n_1$ and $\partial F/\partial \alpha_i$ are not zero, the relaxation process occurs, in which the values of n_1, α_1, and α_2 vary with time and tend to their equilibrium values. Kinetic model for the translocation of a polymer chain can be given by the following three coupled Langevin equations:

$$\zeta_1 \frac{\partial n_1}{\partial t} = -\frac{\partial F}{\partial n_1} + g_1(t), \tag{14}$$

$$\zeta_1 \frac{\partial \alpha_1}{\partial t} = -\frac{\partial F}{\partial \alpha_1} + g_1(t), \tag{15}$$

$$\zeta_2 \frac{\partial \alpha_2}{\partial t} = -\frac{\partial F}{\partial \alpha_2} + g_2(t), \tag{16}$$

where $g_i(t)$ is the Gaussian white noise connected to ζ_i via fluctuation-dissipative theorem, $\langle g_i(t)g_i(0)\rangle = 2\zeta_i k_B T\delta(t)$, $\zeta_i = 6\pi\eta_i R_i$ is a friction constant of a polymer in region i ($=1,2$), η_i shows the viscosity of a solvent in region i.[21] From Eq. (3), the gyration radius R_i of the polymer chain in region $i(=1,2)$ is given by

$$R_i/a = \alpha_i\sqrt{n_i}. \tag{17}$$

Then, the radius R_i is given as a function of n_1 and α_i and the friction constant ζ_i is changed with time. We here assume that $\eta_1=\eta_2$ and neglect the term of the random forces.

In our numerical calculations, we put as most polymer segments are in region 2 at the initial stage: $n_1=1$, $n_0=1$, $n_2=n-n_0-n_1$. As shown in Fig. 2, these conditions are realized when $\chi_2=0.5$ and the value of χ_1 is large (poor solvent) where the value of the expansion factor α_i is about 1.1. We set these values as the initial conditions and take a final stage as $\chi_2=0.5$ and $\chi_1=0$. Figure 3 shows the dimensionless free energy βF, Eq. (1), as a function of n_1 for $\chi_1=0$ and $\chi_1=0.4$ with $\chi_2=0.5$. The values of α_i are determined by Eqs. (9) and (10). The free energy has a minimum which corresponds to the final state, or equilibrium value as shown in Fig. 2(a). With time the relaxation process occurs from the initial state to the final one following the arrow on Fig. 3 and the values of n_1 and α_i tend to their equilibrium values. As shown in Fig. 2(a), at the equilibrium (final) state,

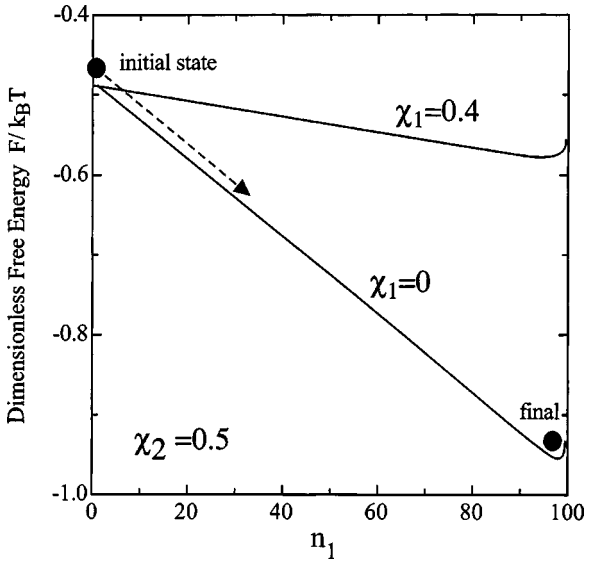

FIG. 3. Dimensionless free energy (βF) as a function of n_1 for $\chi_1=0$ and $\chi_1=0.4$ with $\chi_2=0.5$. The free energy has a minimum which corresponds to the final state. With time the relaxation process occurs from the initial state to the final one following the arrow and the values of n_1 and α_i tend to their equilibrium values.

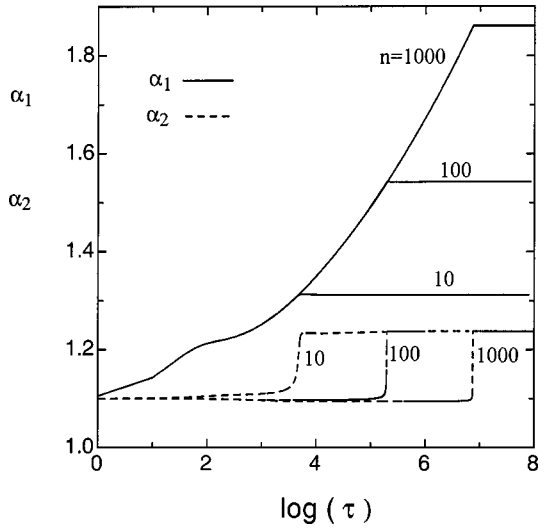

FIG. 5. Time evolution of α_i plotted against the reduced time $\tau=(k_BT/6\pi\eta_1 a)t$ for various value of n. The solid curve shows the expansion factor α_1 and the dotted curve corresponds to α_2.

the polymer segments in region 2 are translocated into region 1. In our numerical calculation we focus on the case of a single-well potential and we do not consider cases with a double-well potential near a phase transition.

Figures 4 and 5 show the numerical results of the time evolution of n_1 and α_i, respectively, plotted against the reduced time $\tau=(k_BT/6\pi\eta_1 a)t$ for various value of n. Note that Fig. 4 shows log-log plot. As shown in Fig. 4, at the initial stage, the fraction n_1 is slowly increased with time and has a power law at the late stage where the time evolution of n_1 is given by $n_1 \propto t^{5/8}$. The value (5/8) of the power is independent of the molecular weight of the polymer. At the late stage, the right-hand side of Eq. (14) becomes almost a constant and so Eq. (14) is given by

$$n_1^{\nu}\frac{\partial n_1}{\partial t}\sim \text{const}, \tag{18}$$

where we have used the friction constant is proportional to $R_1=an_1^{\nu}$. Then we obtain the time evolution of n_1 as

$$n_1 \propto t^{1/(1+\nu)}, \tag{19}$$

for a late stage. When the region 1 is in a good solvent condition ($\nu=3/5$), we get the power law 5/8. In this model the friction constant depends on the radius of the gyration of the polymer in region 1 and 2 (as in the Zimm model[21]). When the friction constant is a constant, n_1 behaves as $n_1 \propto t$ at the late stage. Figure 6 shows the gyration radius R_1 of the polymer chain in region 1 plotted against n_1 for $n=100$. The larger values of n_1 corresponds to the later stages. At the initial stage, the R_1 behaves as $R_1=an_1^{\nu}$, (ν

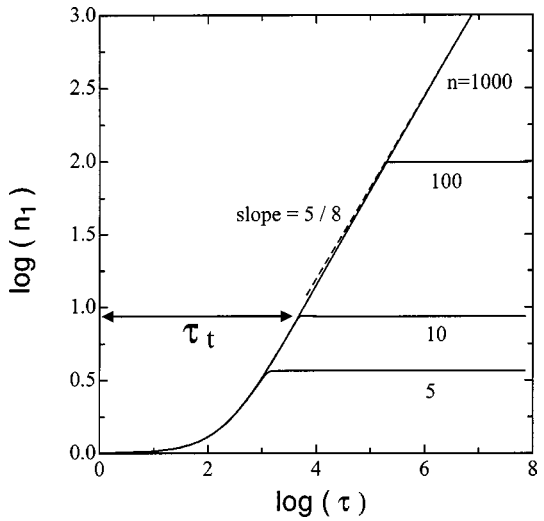

FIG. 4. Time evolution of n_1 plotted against the reduced time $\tau=(k_BT/6\pi\eta_1 a)t$ for various value of n with $\chi_1=0$ and $\chi_2=0.5$. The τ_t shows the translocation time.

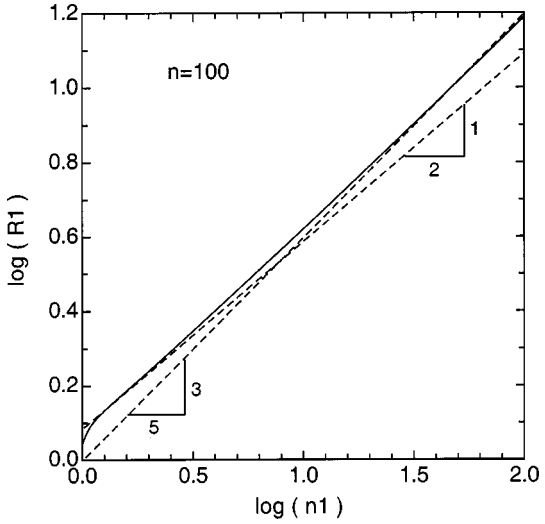

FIG. 6. Gyration radius R_1 of the polymer chain in region 1 plotted against n_1 for $n=100$. The larger values of n_1 corresponds to the later stages where the R_1 behaves as $R_1=an_1^{3/5}$.

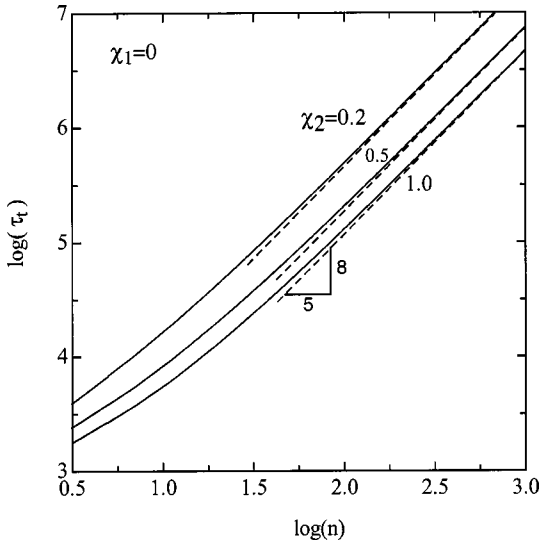

FIG. 7. Translocation time τ_t plotted against the number n of the polymer segments for various values of χ_2 with $\chi_1=0$.

$=1/2$). With time the value of ν is changed from 1/2 to 3/5. Using Eq. (19), we obtain $R_1 \propto t^{3/8}$ at the late stage. The friction coefficient ζ_1 is increased with time.

Figure 7 shows the translocation time τ_t plotted against the number n of the polymer segments for various values of χ_2 with $\chi_1=0$. We here define the translocation time τ_t as the time which satisfies $n_1 \sim n$ as shown in Fig. 4. We find $\tau_t \propto n^{8/5}$ for large n, independent of the solvent condition χ_2. As the solvent condition in region 2 becomes poorer, corresponding to larger values of χ_2, the translocation time becomes shorter. From Eq. (19), the translocation time is given by

$$\tau_t \propto n^{1+\nu}, \tag{20}$$

and we obtain $\tau_t \sim n^{8/5}$ for large n. When the hydrodynamic interaction between polymer segments is neglected as in the Rouse model ($\nu=1$), we have $\tau_t \sim n^2$ which has been obtained by Sung-Park[6] and Muthukumar[8] for large n, using the Fokker-Planck equation for the probability distribution of n_1. Chern *et al.*[10] have performed three-dimentional dynamic Monte Carlo simulation of polymer translocation through a cylindrical pore in a planar slab under the influence of an external driving force with Gaussian chain model. They have shown the translocation time linearly depends on the chain length. When the friction coefficient, or diffusion constant, is independent of the polymer length: $\nu=0$, we get the same scaling behavior.

Figure 8 shows the reduced velocity ($v=1/\tau_t$) plotted against n for various values of χ_2 with $\chi_1=0$. On increasing the molecular weight of the polymer the translocation velocity is decreased. For long polymers the dependence of the translocation velocity on the solvent condition χ_2 is weak, however, for short polymer the velocity increases significantly with increasing the value of χ_2. In recent experiments,[5] the polymer are driven by an external electric field. For polymers longer than the pore length, the translocation velocity is decreased with increasing the length of the polymer and approaches a constant value. Our theoretical results

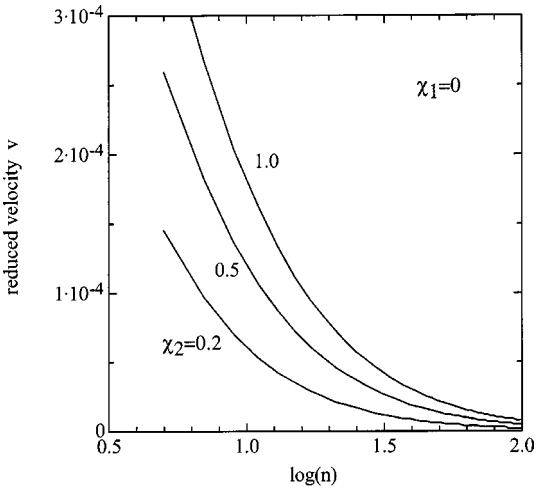

FIG. 8. Reduced velocity ($v=1/\tau_t$) plotted against n for various values of χ_2 with $\chi_1=0$.

are in qualitative agreement with the experiments for long polymers. The similar result has been obtained by a theoretical study based on the Smoluchovskii equation.[13] For short polymers, however, the translocation process is different since there are no polymer segments in the both side of the membrane, as discussed by Slonkina and Kolomeisky[13] We need the extension of our theory to a short polymer chain. In our theory, the difference between χ_1 and χ_2 may correspond to the applied voltage because the solvent condition is changed by current level. We need more explicit treatments of the external electric fields for quantitative agreements and more terms should be added to free energy to account for the applied electric voltage.

Figure 9 shows the time evolution n_1 with $n=100$ for various values of χ_2. For later stages, it behaves as $n_1 \propto t^{5/8}$ which is independent of the solvent condition χ_2. As the solvent condition in region 2 becomes poorer, the time evolution becomes faster. When $\chi_2=0$, it takes an infinite time to translocate the polymer segments into region 1.

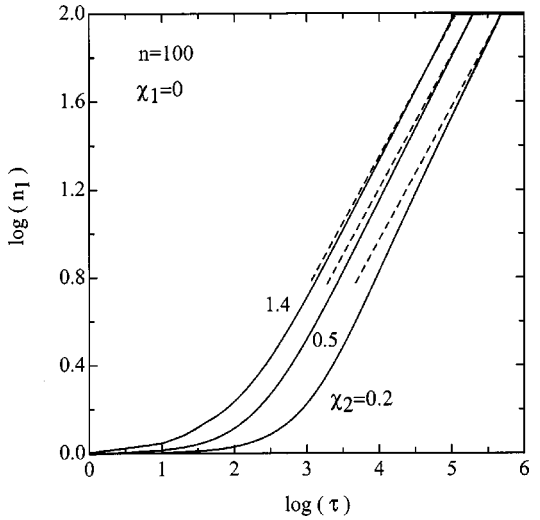

FIG. 9. Time evolution n_1 with $n=100$ for various values of χ_2. For later stages, it behaves as $n_1 \propto t^{5/8}$ which is independent of the solvent condition χ_2.

IV. CONCLUSION

We have theoretically studied the kinetics of a polymer threading through a pore embedded in a membrane. We have numerically solved three coupled kinetic equations for the number n_1 of polymer segments in region 1 and expansion factors of the polymer in both sides of the membrane. When the polymer segments are translocated from region 2 to region 1, we have found the time evolution of the polymer segments as $n_1 \propto t^{1/(1+\nu)}$ and the translocation time τ_t is scaled as $\tau_t \propto n^{1+\nu}$ for large number n of the polymer segments at late stages. When the polymer is translocated into a region 1 with a good solvent condition: $\nu = 3/5$, we obtain $n_1 \propto t^{5/8}$ and $\tau_t \propto n^{8/5}$. As the solvent condition in region 2 becomes poorer the time evolution becomes faster, however, above scaling behavior is independent of the solvent condition of the region 2.

In this paper we have assumed the width of the pore is small and considered that the polymer segments are distributed on both sides of the membrane. We will further study the translocation process without these assumptions. We also emphasis that the translocation process in our model may be experimentally constructed by using different polymer solutions for each side of an impenetrable wall with a pore.[22]

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